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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,498	01/30/2002	Jong-Gu Park	57354-00002	5213

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EXAMINER
SCHULTZ, JAMES

ART UNIT	PAPER NUMBER
1635	6

DATE MAILED: 06/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Fig 6

Office Action Summary	Application No.	Applicant(s)	
	10/066,498	PARK ET AL.	
	Examiner	Art Unit	
	J. Douglas Schultz	1635	

-- Th MAILING DATE of this communication app ars on th cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *12-21 and 24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application/Amendment/Claims

1. Applicant's response filed April 2, 2003 has been considered and fully entered.

Response to Arguments

2. Applicant's election with traverse of group I, claims 1-11, 22 and 23 in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the method of screening gene function of group IV and the method of inhibiting protein or nucleic acid expression of group II require the use of the claimed antisense molecule of group I, and thus groups I, II, and IV are closely related and therefore inseparable. Applicant further argues that the method of making the nucleic acid molecule of group III can be used to make the nucleic acid molecule of group I, so the two groups are thus related by a special technical feature. Finally, applicant argues that it does not require undue experimentation for the examiner to examine the claims because they are so linked, and that it is a burden on applicant to submit multiple applications based on related claims.

This is not found persuasive because applicants' primary argument, that the inventions of groups I-IV involve the use of the same molecule and are therefore inseperably linked, is not the criteria used to determine whether inventions are patentably distinct. As explained in the previous Office action, and as supported by M.P.E.P. § 806.04 and § 808.01, groups are unrelated if they are not disclosed as capable of use together, and have different modes of operation, function, or effects. Groups II and IV have steps that differ completely from one another, and result in different outputs. Restriction is thus proper. Furthermore, M.P.E.P. §

806.05(h) is clear in stating that if the product of one group can be used in a materially different process, the groups are distinct. The products of group I are distinct from the methods of groups II and IV, because as pointed out in the previous office action, the product of group I can be used to assay for gene function, which is different from the method of group II, or alternatively to inhibit gene function, which is different from the method of group IV. Finally applicants' arguments that groups I and III share a special technical feature is not relevant to this application, which is neither a PCT, nor has been filed under 35 U.S.C. § 371 or § 111. Finally, due the non-overlapping method steps and products of these groups, the searches are divergent and non-coextensive. The requirement is still deemed proper and is therefore made FINAL.

Finally, Applicant has included arguments regarding rejoinder. Applicant's attention is directed to the following recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

> "However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

In accordance with M.P.E.P. §821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain

either dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Claims 12-21, and 24-29 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5, filed April 2, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 1, and by dependency, claims 2-11, recite "said antisense molecule". However, there is no literal antecedent basis for "said antisense molecule" in the claim.

4. Claim 1, and by dependency, claims 2-11, are unclear because the metes and bounds of the phrase "specifically binds" cannot be determined. Specific oligo hybridization and binding depends upon many conditions such as temperature, salt concentration, GC content, and oligo length, which applicants have not specifically defined. Thus, the metes and bounds of the nucleic acid probe cannot be determined since applicants have not provided the conditions for determining specific binding.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-7 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is also referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

5. Claim 5, and by dependency claims 6 and 7, are drawn to the large circular nucleic acid molecule according to claim 1, wherein said nucleic acid molecule is a single stranded form of a

recombinant bacteriophage or phagemid genome. Claims 6 and 7 are further drawn to the bacteriophage or phagemid that is derived from a filamentous phage, wherein the phage is phage M13. Claim 9 is drawn to the vector of claim 8 wherein said vector is derived from a filamentous phage.

Applicants disclosure does not provide adequate support for the broad genus of large circular nucleic acids wherein said nucleic acid molecule or is a single stranded *form* of a recombinant bacteriophage or phagemid genome, or wherein said bacteriophage or phagemid or vector is *derived* from a filamentous phage. Specifically, the use of the terms "form" and "derived" in said claims are not defined at all in the specification as originally filed. Furthermore, such terms are considered to be very broad, and encompass an almost unlimited level of variation in the structure of the bacteriophage or phagemid genome that comprises the large circular nucleic acid. As described in the guidelines above, in order to be in possession of a genus with widely variant species, applicants must disclose more than one species within that genus. However, applicants have only described one phage, M13, with no other forms or derivatives of M13, or any other bacteriophage or phagemid. Such a disclosure would not persuade one of skill in the art that applicants were in possession of the broad genus of any single stranded form or derivative of any bacteriophage, phagemid, or vector as claimed.

6. Claim 4 recites the large circular nucleic acid molecule according to claim 1, wherein said antisense region is substantially complementary to an entire gene sequence.

The specification defines the phrase "substantially complementary" as that which is at least 80% complementary to its corresponding target. However, it is well known in the art that even modest mismatches of less than the 20% mismatch instantly claimed by applicant can

completely eliminate antisense activity. As evidence of this, Flanagan et al. is provided, which shows that a 15mer oligonucleotide with 100% complementarity and containing C-5 propyne modifications, which actually *increase* the binding affinity of an oligo for its target (page 2936, 2nd paragraph), could reduce target expression, while a control oligo nucleotide containing 2 mismatches over the length of the 15mer but otherwise identical to the inhibitory oligo (i.e. 87% identical) possessed no antisense-mediated inhibitory activity. Furthermore, applicant has provided no disclosure of any large circular nucleic acid oligos that inhibit target expression and are anything less than 100% complementary to their intended target. Accordingly, because one of skill in the art would be unable to envision oligos containing up to 20% mismatch that retain the function of inhibiting their target, and because applicants have not disclosed any oligos containing any mismatch at all that possess the claimed activity of reducing target expression, one of skill in the art would not be persuaded that applicant was in possession of the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-3, and 5-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Hellmann et al. (Virology. 1985 143:23-34).

The invention of the above claims is drawn to a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said large nucleic acid is about at least about 3000 nucleotides long, or wherein said antisense region is at least about 50 nucleotides long, or wherein said antisense region is substantially complementary to an entire gene sequence, or is a single stranded form of a recombinant bacteriophage or phagemid genome, or is derived from a filamentous phage, which may be M13, or a vector or cell comprising said large circular nucleic acid, or comprises a pharmaceutical carrier, or wherein said circular nucleic acid comprises several antisense regions, that may also comprise a pharmaceutical carrier.

Hellman et al. teach a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said large nucleic acid is about at least about 3000 nucleotides long, wherein said antisense region is at least about 50 nucleotides long, and is a single stranded recombinant bacteriophage that is M13, a cell and a vector comprising said large circular nucleic acid, and wherein said large nucleic acid comprises a pharmaceutical carrier.

2. Claims 1-3, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kool et al. (WO 98/38300).

The invention of the above claims is drawn to a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene,

wherein said large nucleic acid is about at least about 3000 nucleotides long, or wherein said antisense region is at least about 50 nucleotides long, or comprises a pharmaceutical carrier, or wherein said circular nucleic acid comprises several antisense regions, that may also comprise a pharmaceutical carrier.

Kool et al. teach a large circular nucleic acid comprising a target-specific antisense region that specifically binds to a portion of RNA expressed from a gene. Although the large circular nucleic acid of Kool et al. is used primarily as a template for transcribing multiple copies of a ribozyme, the Kool et al. nevertheless indicates that said template comprises a nucleotide sequence complementary to a sequence of interest, which therefore meets the structural limitations of the instant claims. Furthermore, Kool et al. teaches that the antisense region is at least about 50 nucleotides long, and wherein said circular nucleic acid may comprise several antisense regions, that may also comprise a pharmaceutical carrier.

3. Claims 1, 3, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Moon et al. (J Biol. Chem. 2000. 275(18):4647-4653).

The invention of the above claims is drawn to a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said antisense region is at least about 50 nucleotides long that may also comprise a pharmaceutical carrier.

Moon et al. teach a circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is

effective for reducing the expression of said gene, wherein said antisense region is at least about 50 nucleotides long, and comprises a pharmaceutical carrier.

4. Claims 1, 3, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamakawa, H et al. (Nucleosides & Nucleotides, (1995) Vol. 14, No. 3-5, pp. 1149-1152).

The invention of the above claims is drawn to a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said antisense region is at least about 50 nucleotides long,

Yamakawa et al. teach a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said antisense region is at least about 50 nucleotides long.

5. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by LaPlante et al. (Biochem J. 2000. 348:189-199).

The invention of the above claims is drawn to a large circular nucleic acid comprising a target specific antisense region that specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, wherein said antisense region is substantially complementary to an entire gene sequence.

LaPlante et al. teaches a large circular nucleic acid molecule comprising a target specific antisense region that is fully complementary to an entire gene sequence.

Claim Rejections - 35 USC § 103

Claims 1-3, 5-11, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellman et al., in view of Hu et al. (U.S. Patent Number 6,107,062).

The instant invention is discussed above.

The invention of Hellman is as relied upon above. Hellman does not teach the use of a large circular nucleic acid that comprises multiple copies of antisense molecules that are complementary to a plurality of distinct targets.

Hu et al. discloses the use of plasmids containing antisense sequences that target multiple regions of the HIV-1 genome (col. 4, lines 5-15).

It would have been obvious to use the large circular nucleic acids as taught by Hellman et al. and insert multiple antisense nucleic acids directed against distinct targets as disclosed by Hu et al. One would have been motivated to do so because Hu et al. teach that such vectors can be used to effectively inhibit various targets of HIV-1, and because Hellman teach that such circular nucleic acids are effective at avoiding degradation of the circular nucleic acid inhibitor. One of ordinary skill in the art would have had a reasonable expectation of success, because Hellman et al. teach how to insert antisense nucleic acids into large circular nucleic acids, and because inserting more of such sequences is routine to one of ordinary skill. Therefore in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James Douglas Schultz, PhD
June 16, 2003

Karen A Jacourciere
KAREN LACOURCIERE
PATENT EXAMINER